REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the claims

No claims are newly cancelled. Claims 1-13, 15, 24 and 27-39 were previously cancelled. Claims 14, 25 and 26 are amended to recite that the IL-6 antagonist blocks signal transduction of IL-6, and is supported by the specification at paragraph 28 (page 5, lines 30-31). Claims 40 and 41 are new, and parallel claim 14, but recite a method for amelioration of severity of acute pancreatitis and a method for preventing the onset of acute pancreatitis. Claims 40 and 41 are supported by the specification at Examples 1 and 2, particularly paragraphs 126 and 128.

The foregoing amendments add no new matter and are made solely to advance prosecution, without privilege or disclaimer of any subject matter. Following entry of the foregoing amendments, claims 14, 16-23, 25, 26, 40 and 41 are pending, of which claims 14, 25, 26, 40 and 41 are independent.

II. Information Disclosure Statement

The Office asserts that references submitted as exhibits with a response should also be cited in an IDS. Action at page 2. Solely to advance prosecution, Applicant submits herewith an IDS listing all references previously cited by Applicant that have not yet been made of record in an IDS or on Form PTO-892.

III. Enablement rejection

A. The rejection

The Office reasserts the previous enablement rejection of all pending claims. Action at pages 2-6. Whether the art teaches away from a role for IL-6 in pancreatitis is irrelevant if the specification, as filed, is enabling. Therefore, the key issue is how the person of ordinary skill would view the disclosure. According to the Office, the disclosure is not enabling

because the IL-6 antagonist is provided *before* pancreatitis is induced, and therefore is not a working example. More particularly, page 6 of the Action states:

> At page 4 of the response, applicants argue that cerulean-induced acute pancreatitis is an accepted model system. This argument has been fully considered but is not deemed persuasive because in Example 1, the treatment was given before the cerulean was administered, and hence before the acute pancreatitis developed The same is the case in Example 2. Thus the examples are not considered by the Examiner to be "working" examples, as they do not relate to the claimed invention. Such is not the case in the references cited by applicants at page 4 of the response, as characterized by applicants.

Applicant respectfully traverses the rejection as it might have been applied to the pending claims, for reasons of record and further in view of the following comments.

B. Applicant's working example follows the standard of the art

The Office puts great weight on the *timing* of therapeutic intervention, with the assertion that therapeutic intervention before pancreatitis occurs would not be considered to be a "working example." This conclusion is made without reference to, or any evident consideration of, Exhibits G-K that were discussed on pages 5-6 of the previous reply. These references show not only that cerulein-induced pancreatitis is a recognized animal model for human pancreatitis, but also that administration of the drug *before* pancreatitis is considered suitable, *in that model*, for predicting the effectiveness of a drug against pancreatitis per se.

Exhibit I (Michalski *et al.*, *Gastroenterology* 132:1968-1978, 2007) reports administering cannabinoids to mice 30 minutes *before* and 4 hours after administering cerulein (page 2). The authors found that the model mimicked features of human pancreatitis and concluding that their latest findings "demonstrate the *in vivo* significance and therapeutic potential of cannabinoids in inflammation and pain associated with pancreatitis using human specimens and mouse models as test systems." *Id.*

Exhibit H (Yamaguchi *et al.*, *J. Pharmacol Exp. Ther.* 328: 256-262, 2009) describes administration of risperidone at the start of a diet that induced pancreatitis (page 257), and conclude that "Risperidone may provide a new therapy for the disease [pancreatitis]."

As demonstrated by these two exhibits, administration of a drug at, or prior to, the induction of pancreatitis in animal models is considered to be suitable to assess the *therapeutic* effectiveness of the drug in pancreatitis. They are not characterized as being limited only to prophylaxis, but as "treatment" more generally. Because administration of a drug prior to induction of pancreatitis in an animal is considered suitable for measuring the effectiveness of a drug for treatment, the person of ordinary skill would perceive no barrier to enablement of the present claims merely because the specification describes administration of an IL-6 antagonist before induction of pancreatitis.

C. Evidence of preventive efficacy permits claims to therapy

Even if the Office persists in interpreting the data as demonstrating efficacy only of *preventing* disease, this interpretation should not foreclose enablement of the present claims. The antibodies described in the specification have been shown to block IL-6 signal transduction (*see*, *e.g.*, paragraphs 133-137, 147, 148) and were effective in blocking induction of pancreatitis by cerulein. This is the first demonstration of a nexus between IL-6 and acute pancreatitis in an accepted *in vivo* model. Having demonstrated (a) the importance of IL-6 to pancreatitis, (b) that the inhibitor blocks IL-6 signal transduction, and (c) thereby prevents pancreatitis, the person of ordinary skill would accept as reasonable that such intervention would be effective in blocking further IL-6 mediated damage, and thereby suitable for *also* treating on-going disease. That is, regardless of whether an anti-IL-6 receptor antibody is administered prior to or after onset of pancreatitis, an anti-IL-6 receptor antibody blocks signal transmission by IL-6 at any time and can therefore treat acute pancreatitis.

D. Claims 25, 26, 40 and 41 are enabled for additional reasons

Claims 25, 26, 40 and 41 recite methods of "reducing pancreatic edema" "ameliorating the severity of acute pancreatitis" and "preventing the onset of acute

pancreatitis," and therefore encompass a scope that is closer to, if not within, the prophylactic efficacy to which the Office seeks to limit the evidence. *See* Action at page 5. Therefore, these claims, and especially claims 40 and 41, are enabled for reasons that do not apply to claim 14.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

Examiner Spector is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date January 6, 2011 By _____

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